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AWARD NUMBER: W81XWH-14-2-0160

TITLE: Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health, and Physical Performance

PRINCIPAL INVESTIGATOR: Oscar E. Suman, PhD

CONTRACTING ORGANIZATION: The University of Texas Medical Branch at Galveston
Galveston, TX 77555

REPORT DATE: October 2015

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

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REPORT DOCUMENTATION PAGE

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1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
October 2015	Annual	15 Sep 2014 - 14 Sep 2015

4. TITLE AND SUBTITLE
Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health, and Physical Performance

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-14-2-0160

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The University of Texas Medical Branch at Galveston
301 University Boulevard
Galveston, TX 77555-5302

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
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13. SUPPLEMENTARY NOTES

14. ABSTRACT
Prolonged inactivity accompanying stays in the burn intensive care unit (BICU) and hospital worsen muscle loss/weakness and lengthen hospitalization. We hypothesize that a personalized, structured, and quantifiable exercise program (MP10) will improve these variables over standard-of-care (SOC), as exercise has well-documented effects on maintaining/improving muscle strength, which should shorten hospitalization. Thus, we will characterize: (Aim 1) what is SOC throughout hospital stay across the US and (Aim 2) outcomes in burn in-patients. Over 4 years, we will enroll 96 patients (24 per site; MP10 n=64 and SOC n=32) aged 18-60 years with ≥30% TBSA burns. MP10 will begin ~4-5 days after the first surgery after admit (or when the burn surgeon deems mobilization safe) and continue for the entire BICU and hospital stay. MP10 will take place on weekdays in the morning and afternoon. In the morning, patients will participate in a 10-minute leg-crank ergometry session (Monark leg ergometer), starting with a load (watts) eliciting a 3-5 rating on the Borg Rated Perceived Exertion (RPE) scale. The number of revolutions in 10 minutes and minute-by-minute muscle and respiratory effort RPE will be noted. In the afternoon, patients will participate in a 10-minute arm crank ergometry session, which will be done similarly to lower body exercise. Endpoints are lean body mass, cardiopulmonary and muscle endurance, length of BICU, ventilator and hospital stay, and Quality of Life. Within- and between-group comparisons will be performed. A successful MP10 can be a platform for future rehabilitation programs in burns or trauma.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	22	**19b. TELEPHONE NUMBER** *(include area code)*

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TABLE OF CONTENTS

	Page No.
1. Introduction	4
2. Keywords	4
3. Accomplishments	4
4. Impact	6
5. Changes/Problems	8
6. Products	10
7. Participants & Other Collaborating Organizations	12
8. Special Reporting Requirements	14
9. Appendices	15

1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The title of this project is "Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health and Physical Performance". It has four sites: UTMB-Galveston, TX; AISR-San Antonio, TX; UTSW-Dallas, TX; UC-Davis. The prolonged inactivity that occurs in the burn intensive care unit (BICU) and hospital, results in worsening of muscle loss, muscle weakness, and in increased BICU and hospital stay. We need to reduce this time to speed up resuming normal physical activities, returning to work or to professional duties. To this end, we have two aims: **Aim 1**: to characterize, via a survey(s) the Standard of Care of in-patient care (BICUs, on ventilator, step down from BICU) across the U.S. **Aim 2**: to assess the efficacy of a personalized, structured, and quantifiable exercise program (MP10) implemented typically 4 to 5 days after the first surgical operation after admit (or when burn surgeon deems mobilization to be safe), and during the entire BICU, on ventilator and in-hospital stay in burned individuals.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Exercise, burns, standard of care, MP10, early exercise, lean mass, muscle strength, 6 minute walk

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals and objectives of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Milestones:
Aim 1: to characterize, via a survey(s) the Standard of Care of in-patient care (BICUs, on ventilator, step down from BICU) at the 4 sites (UTMB-Galveston, USAISR, UTSW-Dallas, UC Davis)
Due: Y1 Report 14-Oct-2015 Surveys were sent to 4 sites and results were returned from 3. We are waiting for the 4th site (2nd notice sent out OCT 13-2015). Completion Date: 14-Sep-2015

Aim 2: to assess the efficacy of a personalized, structured, and quantifiable exercise program (MP10) implemented typically 4 to 5 days after the first surgical operation after admit (or when burn surgeons deems mobilization to be safe) and during the entire BICU, on ventilator and in-hospital stay in burn individuals. UTMB is enrolling patients and UC Davis is preparing to enroll patients very soon.
Due: Final Report 12-Dec-2018 Completion Date: 14-Sep-2018

Year 1 Key Milestones: Get site ready for study (done); develop individual data forms and survey (done); obtain IRB and HPRO approvals (done); register with clinicaltrials.gov (done). Only USAISR is missing IRB approval at this date.
Due: Y1 Report 14-Oct-2015 Completion Date: 14-Sep-2015

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1) **Major activities**

For Year 1, Q4 Period of June 15, 2015 to September 14, 2015

We focused on recruiting the initial patients at UTMB as the lead site. Then we focused on each site, as well as progressing with Aim 2, (in-patient exercise). The timeline of events are as follows:

- June 15, 2015 the Arm Ergometers were received at UTMB/SHC-Galveston.
- June 26, 2015 the UTSW IRB approval issued.
- June 29, 2015 the Arm Ergometers were assembled at UTMB/SHC-Galveston.
- July 01, 2015 patient screening for study inclusion and recruitment began at UTMB-SHC.
- August 05, 2015, following the meeting of April 21-24, 2015, an improved parent protocol was submitted to the UTMB IRB. (This clarified site names such as SHC-NCA and minor protocol revisions were made which did not affect patient risks.)
- August 08, 2015 the first experimental subject (MP10+SOC) was enrolled at UTMB/SHC-Galveston.
- August 26, 2015 the second experimental subject (MP10+SOC) was enrolled at UTMB/SHC-Galveston.
- Presently there are a total of two subjects enrolled.

SITE by SITE

Study Site: UC-Davis (Dallas, TX) PI – Soman Sen, MD

As of September 17, 2015 UCD/SHC-NCA have IRB approval. Expiration date is 04/12/2016

Study Site: UT Southwestern (Dallas, TX) PI – Karen Kowalske, MD

The study was submitted to the Subcommittee on Human Use of Radiation and received approval. Subsequently IRB approval was issued June 26, 2015.

SA1: Survey on Standard of Care for Burn Patients: Early Exercise and Mobilization in the Burn Intensive care Unit (BICU) was completed September 14, 2015 via Survey Monkey.

Study Site: USAISR PI-Booker King, MD

All activities are being devoted to obtain IRB approval. CRADA has been completed (MAY 20, 2015)

What opportunities for training and professional development has the project provided?

"Nothing to Report."

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

"Nothing to Report." However, quarterly, we do get together with UTSW and USAISR key investigators of this project and discuss progress and issues. The next meeting will take place on November 21 in Dallas and we will attend.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

1. We will analyze results of the surveys that were sent out. We anticipate two abstracts to be prepared. One will be on SOC with and without MP10 in the pediatric burn population and one will be in adults. We will prepare abstracts to be presented at a national/international conferences such as American Thoracic Society (2016 or 17), Critical Care Medicine (2017), International Society for Burn Injuries (2016) or the American Burn Association (2017). Manuscript(s) will follow also in 2016.
2. For Aim2, we will continue to enroll, especially for UCD/SHC-NCA and UTMB/SHC-GAL. We also anticipate enrollment to start very soon at UTSW. We will work very hard to bring USAISR to having full IRB approval (see section on **Actual or anticipated problems or delays and actions or plans to resolve them**).

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

"Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

"Nothing to Report."

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

"Nothing to Report."

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

UTSW and USAISR have had problems obtaining DEXA machines for assessing lean mass. UTSW burn rehab outpatient unit has recently moved and they will be unable to do DEXAs on inpatients while in the BICU. They will be able to do DEXAs as outpatients at the discharge time point. USAISR does not at the present have a DEXA available. On advice of the medical surgeons from UTSW (Dr. Steve Wolf) and UTMB (Dr. David Herndon), UTSW will not be obtaining this measurement while patient is in the ICU. They will only obtain assessment at discharge. We will use multiple imputations for missing data technique at the conclusion of Aim 2.

Due to the opening of the new Dallas County Parkland Hospital there has been a change in location of inpatient burn injury services. This is now separate from the location of the radiology facility which houses the DEXA scanner. Although we will be able to provide most procedures for the study UT Southwestern will not be able to provide the initial DEXA scan. If a DEXA becomes available in the ICU, we will then assess body composition in the ICU (early stage) and at discharge from ICU.

At USAISR there have been numerous changes in personnel. The most noticeable one is that Sandra M. Escolas, PhD left San Antonio to become Director of the US Army Medical Research Unit-West in McChord, WA. She will remain involved, but we will have to communicate via phone, email, etc and not in person. We may be able to meet during conferences or the PI (Dr. Suman) may travel there to discuss key issues related to psychosocial assessments once enrollment has reached ¼ point.

USAISR has not been able to hire a grants coordinator that can focus on the MP10 project. To date Mr. Reginald Richards has been vital and key to the present progress. However, he has not been able to devote much effort to MP10. They are in dire need of a dedicated person for MP10. A therapist has also not been identified and presently the project has not received IRB approval nor is it in consideration to receive IRB evaluation for approval.

More discussions with Dr. Kevin Chung and Dr. Booker King are planned to expeditiously find solutions to these issues at USAISR.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

There is nothing to report for UTMB/SHC-GAL, UTSW and UCD/SHC-NCA. The potential continued shortage of personnel at USAISR specific to the MP10 project may have affected and if continued, will eventually affect expenditures.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

"Nothing to Report."

Significant changes in use or care of vertebrate animals.

"Nothing to Report." And not applicable.

Significant changes in use of biohazards and/or select agents

"Nothing to Report."

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications.

  "Nothing to Report."

  Books or other non-periodical, one-time publications.

  "Nothing to Report."

  Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if*

  "Nothing to Report."

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

  Nothing to Report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

  Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name: *Oscar Suman*
Project Role: *Project Director*
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: *2 calendar months*
Contribution to Project: *Dr. Suman has performed work in the area of preparing protocol and ALL IRB documents and revisions. Dr. Suman has also coordinated communication between USAIR, UC-Davis, and UTSW. Dr. Suman recruited and enrolled the first two experimental MP10+SOC subjects.*

Name: *Michael Serghiou*
Project Role: *Consultant*
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: *not applicable*
Contribution to Project: *Mr. Serghiou has provided guidance to Dr. Suman in the preparation of the protocol revisions to the IRB on exercise in the ICU with greater safety.*

Name: *Jennifer Kemp*
Project Role: *Consultant*
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: *not applicable*
Contribution to Project: *has provided guidance to Dr. Suman in the preparation of the protocol revisions to the IRB on exercise in the ICU with greater safety. In addition she has lead the preparation and sending of the Survey on SOC.*

Name: *Ronald Mlcak*
Project Role: *Consultant*
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: *not applicable*
Contribution to Project: *Dr. Mlcak has provided guidance to Dr. Suman in the preparation of the protocol revisions to the IRB on exercise in the ICU with greater safety.*

Name: *Frank B. Willis*
Project Role: *Physical Therapist/Sr. Clinical Research Coordinator*
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: *2 calendar months*
Contribution to Project: *Dr. Willis assisted with IRB and other regulatory submissions, as well as the preparation of progress reports. He is also in charge of subject enrollment, consenting, and the assessments described in the proposal.*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

See Attachment 1 for changes in active other support.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Organization: University of California – Davis
Location: 1850 Research Park Dr. Ste. 300, Davis, CA 95618-6153
Contribution to the Project: Collaboration

Organization: The University of Texas Southwestern Medical Center at Dallas
Location: 5323 Harry Hines Blvd., Dallas, TX 75390-9105
Contribution to the Project: Collaboration

Organization: US Army Institute of Surgical Research
Location: 3698 Chambers Pass, Ft. Sam Houston, TX 78234-6315
Contribution to the Project: Collaboration

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

9. APPENDICES:

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Attachment 1: Changes to Active Other Support
Attachment 2: IRB Approval

Early Mobility/Exercise Program (MP10) in the Burn Intensive Care Unit (ICU) Decreases Hospital Stay and Fatigue, and Improves Mental Health and Physical Performance

Log 13214039 Award # W81XWH-14-2-0160

PI: Oscar E. Suman **Org: University of Texas Medical Branch/Shriners Hospital-Galveston** **Award Amount:** $1,079,350.00

Study/Product Aim(s)

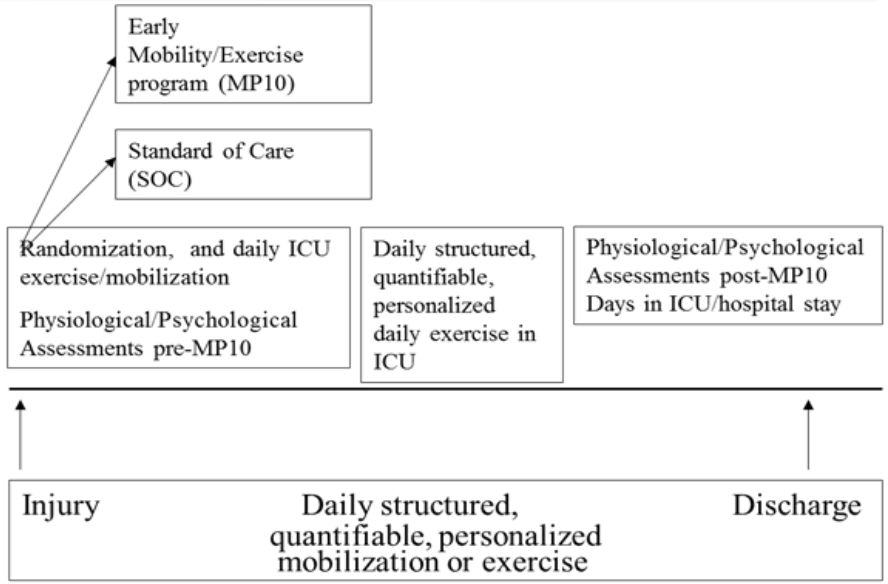
- **Objectives**: 1. decrease length of hospital stay 2. improve physiological and psychological outcomes
- **Aim 1**: Characterize SOC in the ICU in each of the 4 sites.
- **Aim 2**: Test the hypothesis that early exercise in the ICU will significantly improve outcomes compared to SOC.
- **Outcomes**: decreased ICU/hospital stay, improved lean mass, aerobic capacity/muscle endurance and fatigue scores.

Approach

Over 4 years, we will enroll 96 patients (24 per site; MP10 n=64 and SOC n=32) aged 18–60 years with ≥30% TBSA burns. Patients in MP10 will participate in a 10-minute leg-crank and a 10-minute arm crank ergometry session. Endpoints are lean body mass, cardiopulmonary and muscle endurance, length of BICU, ventilator and hospital stay, and Quality of Life.

Timeline and Cost

Activities CY	1	2	3	4
a. Construction and development of Survey to characterize SOC; b. submit for peer-reviewed publication				
Implement MP10+SOC vs SOC, obtain IRB, HRPO, register for clintrials,gov, enroll patients				
Submit manuscripts, present posters or oral presentations				
Estimated Budget ($K)	296,093	254,824	261,734	266,699



Goals/Milestones

CY1 Goal – IRB and HRPO approval for all sites
Survey completion to characterize SOC completed by 4 participating sites

CY2 Goals – MP10 implementation at all sites
Enrollment of patients at all sites; implementation of MP10
Submit abstract or manuscript on Survey to ATS, ABA, ISBI or burn journal

CY3 Goal – Continuation of MP10

CY4 Goal – Continuation of MP10
Analysis of data, submission of abstracts to ABA or other critical care meetings. Submission of manuscript on MP10

Comments/Challenges/Issues/Concerns

- For Y1:4Q, UTMB protocol revisions approved by IRB.
- First 2 patients enrolled at UTMB/SHC-Galveston.

Budget Expenditure to Date (through 9/14/2015)

Projected expenditure: $296,043 (includes sub-awards)
Actual FY1 expenditure: $77,498

Updated: OCT 01-2015

ATTACHMENT 1: CHANGES IN ACTIVE OTHER SUPPORT

Suman, Oscar E

W81 XWH-14-2-0160 (PI: Suman, Oscar E) 09/15/14-09/14/18 13%
Dept of Defense $212,695
"Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health and Physical Performance"
Goal: To obtain a successful, quantifiable exercise program (MP10) which can be a platform for future rehabilitation programs in burns or trauma.
Aims: 1) To characterize what is Standard of Care throughout hospital stay across the US. 2) To characterize outcomes in burn inpatients.
Role: Principal Investigator
Contact: Doug Medcalf, 301-619-2394, douglas.a.medcalf.civ@mail.mil
Overlap: This is the grant for which the progress report is being submitted.

#71006 (PI: Suman, Oscar E) 01/01/12-12/31/16 4%
Shriners Hospitals for Children $121,965
"Amino acid supplementation in recovery from severe burn"
Goal: To determine if amino acid supplementation combined with exercise training leads to greater improve¬ments in liver and plasma lipid concentrations, muscle lipid metabolism, and insulin resistance, than exercise alone during rehabilitation in burn children.
Aims: In these aims, we will determine if EAA supplementation combined with exercise training yields greater improvements in the following outcomes than exercise alone:
1) liver and plasma triglyceride (TG) concentrations;
2) muscle lipid metabolism (fat oxidation, concentrations of TG and fatty acid intermediates, number of mitochondria and mitochondrial oxidative capacity);
3) insulin resistance.
Role: Principal Investigator
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728
Overlap: None

#71008 (PI: Herndon, David N) 01/01/12-12/31/16 5%
Shriners Hospitals for Children $119,025
"Mechanisms of Improved Wound Healing & Protein Metabolism of Insulin & Metformin"
Goal: To understand the mechanisms by which insulin and metformin can improve wound healing and protein metabolism.
Aims: 1) Determine how insulin and metformin affect whole-body and organ function post burn on a clinical level. 2) Determine the mechanisms whereby insulin and metformin exert their effects post burn on a cellular level
Role: Co-Investigator
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728
Overlap: None

#71009 (PI: Suman, Oscar E) 01/01/12-12/31/16 12%
Shriners Hospitals for Children $144,806
"Oxandrolone and propranolol will promote recovery in the severely burned"
Goal:
Aims: The following aims will allow the testing of the major hypothesis.
Aim 1: Is to test the hypothesis that the catabolic (lean mass, protein synthesis and protein breakdown) response can be ameliorated by therapeutic use of the testosterone analog, oxandrolone combined with the therapeutic use of the propranolol over a treatment period of 1 year.
Aim 2: Is to test the hypothesis that the hypermetabolic (heart rate, blood pressure, resting energy expenditure) response can be ameliorated by therapeutic use of the testosterone analog, oxandrolone combined with the therapeutic use of the propranolol over a treatment

period of 1 year.
Aim 3: To identify factors (cytokines in blood and urine) and potential mechanisms involved in these hypermetabolic and catabolic process in response to the administration of both treatment drugs. We will determine whole-body physiologic changes, as well as clinical, and biochemical changes over the 1 year study period.
Role: Principal Investigator
Contact: Carole Miller, Shriners Hospitals for Children, 409-770-6728
Overlap: None

P50 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 15%
National Institutes of Health $191,873
"Mitigation of the Catecholamine Surge in Severely Burned Patients"
This is a program project grant that will study the efficacy, effects and mechanisms of the reduction in post-burn catecholamine surge by the non-selective beta-1 and beta-2 adrenergic antagonist, propranolol, in severely burned children and adults.
Project Title: Project 1: Propranolol Effects, Clinical Outcomes and Quality of Life in the Severely Burned
Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials
Aims: 1) To determine the effects of long-term propranolol administration on cardiac work as reflected by the product of heart rate and mean arterial blood pressure, and resting energy expenditure as reflected by resting oxygen consumption; 2) To determine the effects of long-term propranolol administration on muscle mass and muscle function, as reflected by lean body mass index and peak strength; 3) To assess changes in key biomarkers of inflammation and infection (C-Reactive Protein and Interleukin-6) in response to the long-term administration of propranolol; 4) To determine if propranolol administration improves psychosocial health (Quality of Life) when assessed one year post burn
Role: Principal Investigator
Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov
Overlap: None

P50 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 8%
National Institutes of Health $118,743
"Mitigation of the Catecholamine Surge in Severely Burned Patients"
Project Title: Core A: Administrative Core
Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials
Aims: To function as the administrative and organizational structure that coordinates the activities of the Research Center and facilitates its scientific mission
Role: Core Director
Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov
Overlap: None

P50 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 2%
National Institutes of Health $209,515
"Mitigation of the Catecholamine Surge in Severely Burned Patients"
Project Title: Core C: Human Subjects Core
Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of

whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials

Aims: To enroll patients, gather clinical data and measurements, and oversee the acquisition, compilation, and dissemination of all clinical and biolgical data, as well as to collect, catalogue, and distribute patient samples, and to perform basic protein and genetic analyses

Role: Co-Investigator

Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov

Overlap: None

******End date extended.******

W81XWH-09-2-0194 (PI: Wolf, Steven E) 09/30/09-10/29/16 2%

American Burn Association $188,414

"Community-Based Exercise Rehabilitation in Severely Burned Adults"

Goal: To assess the efficacy of implementing a 12-week structured and supervised community-based exercise program (COMBEX) started at hospital discharge.

Aims: The central hypothesis of this proposal is that exercise-induced physical and psychosocial benefits obtained during a supervised and structured community-based exercise program in severely burned adults will improve physical function, and quality of life relative to the Standard of Care.

Role: Principal Investigator

Contact: Susan M. Browning, MPH, Deputy CEO and COO, 312-642-9260

Overlap: None

******New award on 8/5/2014.******

R01 GM056687 (PI: Herndon, David N) 08/05/14-04/30/18 2%

National Institutes of Health $696,523

"Mechanisms of fenofibrate alone or combined with propranolol in burned patients"

Goal: This long-term clinical trial will advance the understanding of burn-induced tissue-specific signaling pathways, alterations in clinical indices such as insulin resistance, body composition, and scarring, and may
improve clinical outcomes of burn patients, and by extension also improve these in other hypermetabolic and hypercatabolic states.

Aims: Aim 1: will characterize the effects of fenofibrate and propranolol on muscle protein metabolism, regional lipid metabolism, and insulin resistance, after severe burn. Aim 2a: will test the efficacy of these agents on wound closure, wound infection, graft rejection, and scarring
(the modified Vancouver and Seattle scar scales). Aim 2b, will determine whether these agents alter wound protein turnover and healing rates by using stable isotope techniques. Aim 2c, will use fibroblasts isolated from skin and scar biopsies to study molecular signaling pathways related to wound healing and scar development. Aim 3: will test the hypothesis that the mechanistic results of SA1 and SA2 are highly associated with improvements in outcomes vital in the acute stage: inflammatory response as reflected by interleukin-6, as well as result in improvements in long term outcomes: lean body mass, resting energy expenditure, cardiac function and quality of life.

Role: Co-Investigator

Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov

Overlap: None

******New award on 1/15/2015.******

1 R01 GM112936-01 (PI: Finnerty, Celeste) 01/15/15-12/31/19 5%

National Institutes of Health $259,620

"Effects of Chronic Catecholamine Exposure on Post-burn Scarring"

Goal: Understanding the mechanisms underlying aberrant wound healing and scarring, and their reversal by propranolol, will lay the foundation to develop additional anti-scarring therapies

for the severely burned.
Aims: Aim 1. Determine the effects of chronic catecholamine exposure and β-blockade on wound healing and hypertrophic scars. Aim 2. Quantitate the effects of β-blockade on scar composition. Aim 3. Determine the effects of β-blockade on β-AR expression, activity, and binding partners of dermal fibroblasts.
Role: Co-Investigator
Contact: Tseng, Hung H., 301-496-0810, tsengh@mail.nih.gov
Overlap: None.

******This is a competing renewal for a previously reported award.******

2 R01 HD049471-10 (PI: Suman, Oscar E) 02/01/15-01/31/20 19%
National Institutes of Health $372,860
"Oxandrolone and Exercise: A Potent Therapy in the Rehabilitation from Burns"
Goal: To identify evidence-based therapeutic interventions that are clinically effective in the rehabilitation and recovery of severely burned children.
Aims: 1) To determine the physiological therapeutic efficacy of exercise training/rehabilitation plus oxandrolone relative to exercise alone; 2) To determine the biochemical consequences of combined exercise training/rehabilitation and oxandrolone relative to those of exercise alone.
Role: Principal Investigator
Contact: Valerie Maholmes, valerie.maholmes@nih.gov, 301-496-1514, 6100 Executive Blvd, Rockville, MD 20852
Overlap: None

******This is a reissue of a previous award (H133A120091) when the granting agency (NIDRR) was transferred from ED to DHHS (as NIDILRR).******

90DP0043-02-00 (PI: Herndon, David N) 04/01/15-09/29/17 2%
National Institute on Disability, Independent Living, and $298,400
"Modulation of catabolism mediated by catecholamine in severely burned children: Analysis of outcomes at hospital discharge, 6 months, 1, 2, 5, 10, 15 and 20 years post-injury"
Goal: This Pediatric Burn Center will conduct clinical research studies that aim to modulate the catabolic and hypermetabolic response to burn trauma and improve long-term burn outcomes in children
Aims: We propose to assess in children with severe burns: 1) the efficacy of propranolol administered for 1 year post-burn to diminish the effects of catecholamine to reduce the hypermetabolic and catabolic response 2) the efficacy of the combination of oxandrolone plus propranolol administered for 1 year post-burn to diminish the effects of catecholamine to reduce the hypermetabolic and catabolic response.
Role: Co-Investigator
Contact: Cate Miller, Administration for Community Living, One Massachusetts Ave, Washington, DC 20201-1401, 202-357-1000
Overlap: None

******New award on 7/1/2015.******

W81XWH-15-1-0143 (PI: Branski, Ludwik) 07/01/15-06/30/19 5%
Dept of Defense $384,660
"Growth Hormone Therapy for Muscle Regeneration in Severely Burned Patients"
Goal: To determine whether restoration of depleted GH levels post-burn will lead to prevention of lean body mass loss and bone mineral content, improve rehabilitation, and accelerate reintegration of severely burned patients.
Aims: To determine the effects of recombinant human growth hormone (rhGH) supplementation on body composition, such as lean body mass loss and bone mineral content, and to assess if rehabilitation and subsequent reintegration of severely burned patients into society can be accelerated.
Role: Co-Investigator
Contact: Darrell L. Beaver, 301-619-2195, darrell.l.beaver4.civ@mail.mil
Overlap: None

******New intramural award on 9/1/2015.******

2014-667 Suman MPI Pilot (PI: Suman, Oscar E) 09/01/15-08/31/16 1%
Univ of Texas Medical Branch $50,000
"Role of Satellite Cells in the Regeneration and Recovery of Skeletal Muscle after Burn Injury"
Goal: To establish a mechanistic role for skeletal muscle resident stem cells (satellite cells) in the muscle respose to burn injury
Aims: 1. Determine the effect of satellite cell depletion on muscle recovery following burn injury. 2. Determine the affect of aerobic exercise on satellite cell content and muscle recovery in pediatric burn patients.
Role: Principal Investigator
Contact: Barbara H. Petit, 409-772-1285, bhpetit@utmb.edu
Overlap: None

******Funding Ended.******

W81XWH1220086 (PI: Enkhbaatar, Perenlei) 09/14/12-09/13/15
DOD $225,503
"Nebulized epinephrine in burn and smoke inhalation injury"

Lee, Jong

W81 XWH-14-2-0160 (PI: Suman, Oscar E) 09/15/14-09/14/18 1%
Dept of Defense $212,695
"Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health and Physical Performance"
Goal: To obtain a successful, quantifiable exercise program (MP10) which can be a platform for future rehabilitation programs in burns or trauma.
Aims: 1) To characterize what is Standard of Care throughout hospital stay across the US. 2) To characterize outcomes in burn inpatients.
Role: Co-Investigator
Contact: Doug Medcalf, 301-619-2394, douglas.a.medcalf.civ@mail.mil
Overlap: This is the grant for which the progress report is being submitted.

P50 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 4%
National Institutes of Health $209,515
"Mitigation of the Catecholamine Surge in Severely Burned Patients"
This is a program project grant that will study the efficacy, effects and mechanisms of the reduction in post-burn catecholamine surge by the non-selective beta-1 and beta-2 adrenergic antagonist, propranolol, in severely burned children and adults.
Project Title: Core C: Human Subjects Core
Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials
Aims: To enroll patients, gather clinical data and measurements, and oversee the acquisition, compilation, and dissemination of all clinical and biolgical data, as well as to collect, catalogue, and distribute patient samples, and to perform basic protein and genetic analyses
Role: Co-Investigator
Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov
Overlap: None

P50 GM060338-14 (PI: Herndon, David N) 09/15/12-08/31/17 1%
National Institutes of Health $186,656

"Mitigation of the Catecholamine Surge in Severely Burned Patients"
Project Title: Project 9: Effects of Propranolol on Hypermetabolism
Goal: This NIH-defined Phase II, intent-to-treat, clinical trial will allow assessment of the effects of propranolol on many organ systems affected by the catecholamine surge, determination of whether blocking the stress response is beneficial or harmful, determination of the molecular mechanisms, determination of whether a full year of treatment is tolerable to most patients, and establishment of a treatment protocol with high compliance rates for future expansion into multi-center trials
Aims: 1) To define the short- and long-term effects of propranolol on a) the development of hepatic steatosis, b) the rate of peripheral lipolysis and systemic FFA availability, and c) very low density lipoprotein-triglyceride (VLDL-TG) kinetics in severely burned patients; 2) To define the short- and long-term effects of propranolol on muscle protein synthesis and breakdown rates, and b) elucidate the mechanisms responsible for the observed propranolol induced alterations in muscle protein metabolism in severely burned patients; 3) To determine the correlations between changes in hepatic steatosis and muscle protein metabolism with changes in body composition and energy expenditure, insulin resistance, and inflammation
Role: Co-Investigator
Contact: Scott D. Somers, PhD, Program Official, 301-594-3827, somerss@nigms.nih.gov
Overlap: None

******New award on 7/1/2015.******
W81XWH-15-1-0143 (PI: Branski, Ludwik) 07/01/15-06/30/19 2%
Dept of Defense $384,660 CL
"Growth Hormone Therapy for Muscle Regeneration in Severely Burned Patients"
Goal: To determine whether restoration of depleted GH levels post-burn will lead to prevention of lean body mass loss and bone mineral content, improve rehabilitation, and accelerate reintegration of severely burned patients.
Aims: To determine the effects of recombinant human growth hormone (rhGH) supplementation on body composition, such as lean body mass loss and bone mineral content, and to assess if rehabilitation and subsequent reintegration of severely burned patients into society can be accelerated.
Role: Co-Investigator
Contact: Darrell L. Beaver, 301-619-2195, darrell.l.beaver4.civ@mail.mil
Overlap: None

******Effort ended on 9/26/2015.******
W81XWH-12-1-0429 (PI: Enkhbaatar, Perenlei) 09/27/12-09/26/16
Dept of Defense No-cost extension
"Vitamin E Supplementation in Burn Patients"

utmb Health
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Institutional Review Board
301 University Blvd.
Galveston, TX 77550-0158
409.266.9475

14-Oct-2015

MEMORANDUM

TO: Oscar E. Suman, PhD
Surgery - Burn Rt. 1220

FROM: Aristides Koutrouvelis, MD
Institutional Review Board, Chairman

RE: Continuing Study Approval

IRB #: IRB # 14-0432

TITLE: Randomized, Controlled, Multicenter Study of the Effect of In-Patient Exercise Training on Length of Hospitalization, Mental Health, and Physical Performance in Burned Patients

DOCUMENTS: Protocol – version dated 08-Jul-2015
English Research Consent Form – version dated 04-Sept-2014
Spanish Research Consent Form – version dated 04-Sept-2014
English Child Assent Form – version dated 07-Sept-2014
Spanish Child Assent Form – version dated 04-Sept-2014
English Parental Permission Form – version 3 dated 10-Dec-2014
Spanish Parental Permission Form – version 3 dated 10-Dec-2014

The UTMB Institutional Review Board (IRB) reviewed the above-referenced research protocol at a convened meeting on 09-Oct-2015. Having met all applicable requirements, the research protocol is approved for continuation for a period of 12 months. The approval period for this research protocol begins on 09-Oct-2015 and lasts until 09-Oct-2016.

The research protocol cannot continue beyond the approval period without continuing review and approval by the IRB. In order to avoid a lapse in IRB approval, the Principal Investigator must apply for continuing review of the protocol and related documents before the expiration date. A reminder will be sent to you approximately 90 days prior to the expiration date.

The approved number of subjects to be enrolled is 24. The IRB considers a subject to be enrolled once s/he signs a Consent Form. If, additional subjects are needed, you first must obtain permission from the IRB to increase the approved sample size.

If you have any questions related to this approval letter or about IRB policies and procedures, please telephone the IRB Office at 409-266-9475.

General Instructions

To maintain IRB approval in good standing, please observe the following requirements:

1. The research consent form(s) (if applicable) with the date of the IRB approval is available in infoED. Please use the IRB stamped consent form(s) with the current approval/expiration dates and make additional copies as they are needed.
2. All subjects must sign the consent form before undergoing any research study procedures, including screening procedures unless this requirement has been waived by the IRB. When conducting research involving children, a child assent form must be reviewed with and signed by the child (if applicable) in addition to obtaining a signed parental permission form unless these requirements are waived by the IRB. A photocopy of the signed consent form(s) should be given to each participant. The copy of the consent form(s) bearing original signature(s) should be kept with other records of this research for at least six years past the completion of the research study.
3. Obtain prior IRB approval for any modifications including addition of new recruiting materials, changes in research personnel or site location, sponsor amendments or other changes to the protocol or associated documents. Only those changes that are necessary to avoid an immediate apparent hazard to a subject may be implemented without prior IRB approval.
4. Report all adverse events, protocol violations, DSMB reports, external reports and study closures promptly to the IRB.
5. Make study records available for inspection. All research-related records and documentation may be inspected by the IRB for the purpose of ensuring compliance with UTMB policies and procedures and federal regulations governing the protection of human subjects. The IRB has authority to suspend or terminate its approval if applicable requirements are not strictly adhered to by all research study personnel.
6. When enrolling subjects who do not speak or read English, in research involving therapeutic or prophylactic interventions or invasive diagnostic procedures, a bilingual translator must be continuously available to facilitate communications between research personnel and a subject. If a bilingual translator will not always be available, it may be unsafe for an otherwise eligible candidate to participate in the research if that person does not speak and read English.